The Turkish Journal of Pediatrics 2023; 65: 801-808
https://doi.org/10.24953/turkjped.2023.240

Original Article

The etiologies and management of spinal cord compression in childhood cancers: Are we aware of the emergency of cord compression?

Arzu Okur, Özge Vural, Faruk Güçlü Pınarlı

Division of Pediatric Oncology, Department of Pediatrics, Gazi University School of Medicine, Ankara, Türkiye.

ABSTRACT

Background. The spinal cord compression causes irreversible long-term permanent neurological sequelae. This study aims to increase awareness of childhood cancers that cause cord compression by comparing histopathological diagnosis, treatments, and survival rates to the literature.

Methods. Seventy-three patients (38 male, 35 female) with spinal cord compression, among 1085 patients diagnosed with solid tumors at Gazi University Department of Pediatric Oncology between 1991 and 2021 were retrospectively evaluated.

Results. The mean time between the onset of complaints and diagnosis was 27.5± 24.9 (2-150) days. The first three most common tumors that caused cord compression; were central nervous system tumors in 22 (30%), neuroblastoma in 17 (23%), and malignant germ cell tumors in 8 (10%) cases. Of the patients, 46 (63%) had compression due to extradural masses, and 27 (37%) patients had an intradural compression. The most common symptoms were pain in 60 (82%), weakness in 57 (78%), and pins and needles in 28 (38%) patients, respectively. The clinical physical neurological examination findings were motor deficit in 62 (84%), and deep tendon reflex changes in 54 patients (73.9%). Compression findings were detected in 58 (79.5%) patients at diagnosis, and in 15 (20.5%) of them during follow-up. The most common level of compression was seen in the thoracolumbar region in 19 (26%) cases. In 65 (89%) patients with cord compression, corticosteroids were given as anti-edema treatment. Surgical excision was performed in 39 (53%) patients. Spinal radiotherapy was given to 35 patients (48%) with radiosensitive tumors. Chemotherapy protocols were started in 52 (71.2%) cases according to their diagnoses. Complete neurological recovery was achieved in 33 (45%) patients. The 5-year overall survival rates for solid tumors with extradural compression and intradural compression were 62% and 22%, respectively (p=0.002).

Conclusions. Neurological sequela-free recovery is possible with early diagnosis and urgent treatment. Spinal compression must be detected by detailed systemic and neurological examination and imaging methods. Patients should be rapidly transferred to pediatric oncology units after starting anti-edema treatment.

Key words: spinal cord compression, childhood cancers.

The spinal cord, conus medullaris or cauda equina compressions impair quality of life and cause irreversible, long-term, permanent neurological sequelae. The spinal cord may be compressed by a mass in the epidural space (extradural), or by metastatic spread to the cord parenchyma (intradural).[1,2] Although the incidence of acute cord compression may vary depending on the histopathology of the tumor, findings of cord compression occur in approximately 4-5% of childhood cancers at diagnosis.[1] While these rates in neuroblastoma, and in Hodgkin lymphoma were 9%, and 2% respectively, it was reported as 11-43% in medulloblastoma, at diagnosis.[1,3,4] In childhood

✉ Arzu Okur
arzu-okur@hotmail.com

Received 3rd April 2023, revised 7th July 2023, 27th August 2023, accepted 30th August 2023.

cancers, patients may only present with symptoms of cord compression.

Back pain is the most common presenting sign of spinal cord compression. Neurologic findings may vary depending on the spinal level of the lesion and the degree of compression. Weakness, ataxia, gait disturbance, and paraplegia can be observed. Sphincter dysfunction is seen most commonly as urinary retention or constipation. The localization of the level of epidural cord compression along the spine is determined by the specific effects on extremity strength, tendon reflexes, and sensory levels.[5-7] Treatment options for a patient with spinal cord compression include surgery (laminectomy or laminotomy), chemotherapy, anti-edema (steroid) therapy, and radiation therapy.[7]

The histopathology of the tumor is important in the choice of treatment for tumor-related cord compression. However, early and immediate interventions are essential, as is histopathology for complete recovery without neurological sequelae. Since most childhood malignant tumors are chemosensitive, complete neurological recovery can be achieved with rapid and appropriate treatment of the malignancy in pediatric cancer patients.[5,8]

This study aims to increase awareness of childhood cancers that cause cord compression by comparing histopathological diagnosis, treatment results, and survival rates to the literature.

Material and Methods

The clinical and demographic features, pathological characteristics, treatment modalities, survival rates, and functional neurological outcomes of pediatric patients who developed cord compression due to solid tumors at Gazi University, Department of Pediatric Oncology between 1991-2021 were evaluated retrospectively. This study was approved by the Ethics Committee of Gazi University (No. 2017120103-2).

Statistical analysis

Quantitative data were represented by mean ± standard deviation. Percentages described qualitative data and the comparison of these data was performed using the chi-square test. Patient and disease characteristics were compared between groups using Mann-Whitney U and chi-square/Fisher tests for numerical and categorical variables, respectively. Kaplan-Meier survival analysis was used to assess the median survival probability. Patient groups were compared in terms of survival duration using a log-rank test. All analyses were performed using SPSS 21.0 software (SPSS, Inc., Chicago, IL, USA), and $p<0.05$ was considered statistically significant.

Results

We retrospectively evaluated 73 patients (38 male, 35 female) with spinal cord compression out of 1085 patients diagnosed with solid tumors at Gazi University Department of Pediatric Oncology between 1991 and 2021. Cord compression was present in 6.7% of all childhood malignant tumors at our pediatric oncology unit. Patients with leukemia were not included in this study. The demographic findings of the patients including gender, age at diagnosis, duration of symptoms, and follow-up periods have been shown in Table I.

Table I. Distribution of patients by demographic findings.

		Patients (n:73)
Gender	Male	38 (52.1%)
	Female	35 (47.9%)
Age (years), mean ± SD (range)		4.92 ± 4.46 (0.31-16.27)
Symptom duration (days), mean ± SD (range)		27.5 ± 24.9 (2-150)
Follow-up period (years), mean ± SD (range)		3.26 ± 4.90 (0.1-22)

SD: standard deviation

In this study, 46 (63.1%) patients had extradural, and 27 (36.9%) patients had intradural cord compression. Spinal cord compression was observed in 58 (79.5%) patients at diagnosis and in 15 (20.5%) patients at relapse or progression. Twenty-two patients with intradural compression had central nervous system (CNS) tumors (medulloblastoma, astrocytoma, ependymoma), and 12 of them developed cord compression in progression or relapse. The histopathological diagnosis of patients and levels of cord compression are shown in Table II. The most common symptoms of the patients were pain in 60 (82%), weakness in 57 (78%), pins and needles in the extremities in 28 (38%), and urinary retention or constipation in 8 (10.9%) cases. The neurological examination findings were motor deficit (paralysis or plegia) in 62 (84%), deep tendon reflex changes or presence of pathological reflex in 54 (73.9%), sensory deficit in 13 (17%), sphincter dysfunction in 8 (10.9%), and tilt in 2 (2.7%) of the patients.

Compression findings of all patients were demonstrated by spinal magnetic resonance imaging (MRI) or vertebral computed tomography. Treatment modalities such as corticosteroids, chemotherapy, radiotherapy, and surgery were applied according to the diagnosis and clinical features of the patients. Approximately 90% of the patients received dexamethasone as an anti-edema treatment. Fifty-two patients (71%) promptly received chemotherapy protocols appropriate for their histopathological diagnosis. Radiotherapy was given to the spinal compression area of 35 patients who showed progression in neurological findings under chemotherapy. As a diagnostic surgical intervention, primary decompressive tumor excision and laminectomy were performed in 26 patients. The treatment modalities applied to the patients are listed in Table III.

When the neurological findings of 73 patients were evaluated after treatment, complete neurological remission was achieved in only 33 (45.2%) patients (Table IV).

Table II. Clinical features of malignant spinal cord compression.

Histopathological diagnosis	Number (%)
Central nervous system tumors	22 (30.1)
• Medulloblastoma	14 (19.1)
• Astrocytoma	6 (8.2)
• Ependymoma	2 (2.7)
Neuroblastoma	17 (23.2)
Malignant germ cell tumor	8 (10.9)
Ewing sarcoma/PNET	7 (9.5)
Langerhans cell histiocytosis	6 (8.2)
Rhabdomyosarcoma	6 (8.2)
Primary spinal cord tumors	5 (6.8)
Burkitt lymphoma	2 (2.7)
Levels of spinal cord compression	
• Cervical	9 (12.3)
• Cervicothoracic	12 (16.4)
• Thorax	18 (24.6)
• Thoracolumbar	19 (26.0)
• Lumbar-sacral	15 (20.5)

PNET: primitive neuroectodermal tumor

Table III. The treatment modalities applied to the patients.

Treatment	Number (%)
Corticosteroid	65 (89.0)
Chemotherapy	52 (71.2)
Surgery	39 (53.4)
• Primary decompressive tumor excision + laminectomy	26 (35.6)
- Complete	13
- Partial	9
- Biopsy	4
• Delayed surgery after chemotherapy	11
• Laminotomy	2
Radiotherapy	35 (47.9)

Table IV. Functional outcomes of 73 patients with malignant spinal cord compression.

Functional Outcomes	Number (%)
Neurological complete recovery	33
Motor deficit	
• Unable to walk	15
• Walking with support	15
Spinal deformity	6
Sphincter dysfunction	4

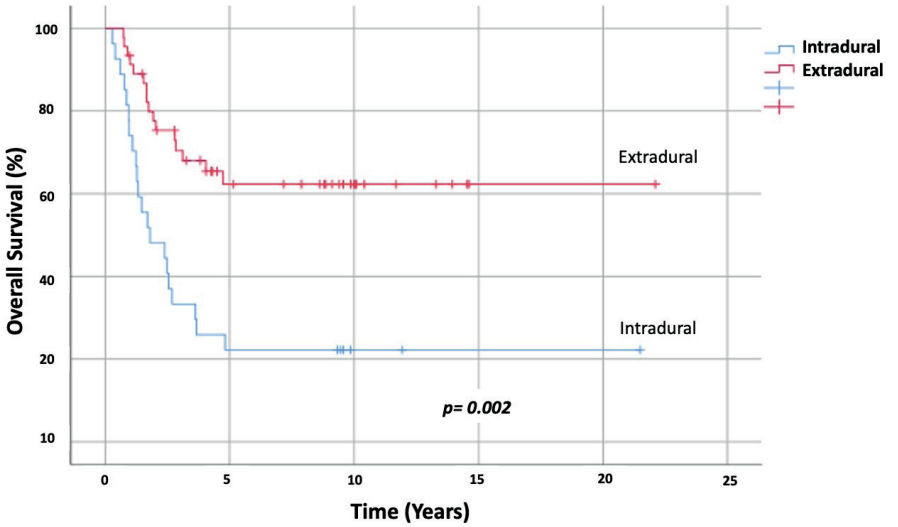

Fig. 1. The 5-year overall survival rates for patients with extradural compression and intradural compression.

While primary CNS tumors (22 patients) were the most common tumor with intradural cord compression, neuroblastoma (17 patients) was the most common solid tumor with extradural cord compression. Of the patients with neuroblastoma, 10 out of 17 were disease-free and in remission, and 7 out of the 10 patients had a complete neurological recovery. Disease-free remission and complete neurological recovery were achieved in 21 out of 46 patients with extradural cord compression. But most of the patients (18) with intradural compression died due to the rapid progression of the disease. When the survival analyses of all 73 patients in this study were evaluated, the 5-year overall survival rates for extradural compression and intradural compression were 62% and 22%, respectively (Fig. 1). Survival rates were significantly higher in patients with extradural tumors of spinal cord compression (p=0.002).

Discussion

The spinal cord, conus medullaris or cauda equina compressions impair quality of life and cause irreversible, long-term, permanent neurological sequelae. Tumor compression on the vertebral venous plexus causes vasogenic cord edema, venous hemorrhage, and ischemia, resulting in tissue damage and neurological deficit.[1,2] Cord compression is classified as extradural or intradural.[9,10] Extradural compression occurs due to the extension of paravertebral tumors through the intervertebral foramina. Extradural masses in children are usually caused by tumors such as neuroblastoma, Ewing sarcoma, rhabdomyosarcoma, lymphomas, germ cell tumors, and Langerhans cell histiocytosis.[11-13] Neuroblastoma is the most common extracranial solid tumor in childhood. It has been reported in various studies in the literature that approximately 10% of neuroblastoma cases have findings of compression at the time of diagnosis.[3,8,14] Seventeen (20%) out of 85 patients with neuroblastoma diagnosed in our center had neurological findings related to epidural compression. Neuroblastoma cases with compression findings were at a higher rate than in the literature in our group. We believe that it is important to raise the awareness of neurologic findings in childhood solid tumors in our country. De Martino et al.[2] reported that the leading cause of cord compression at the time of diagnosis was extradural tumors most commonly neuroblastoma (27.2%) followed by Ewing sarcomas (15.9%). As in the literature, the most common extradural compression tumors were neuroblastoma (23%), germ cell

tumor (11%), and Ewing sarcoma (10%) in the present series. Primary CNS tumors usually cause intradural compression through dropped metastases.[15-17] Primary CNS tumors were the most common malignancy in our series, probably due to being one of the referral centers for pediatric neurosurgery in the country. As primary high-grade CNS tumors with spinal metastases have a poor prognosis, 18 out of 22 patients with CNS tumors died due to the progression of the disease in this study.

Back pain or extremity pain due to tumor compression are usually the first and most prominent symptoms. Pain may be accompanied by motor and/or sensory deficits according to the compression area.[9,18] In the literature, Gunes et al.[11] reported that the most common symptom was pain (64%), and the most common finding on physical examination was motor deficit (53%) in 28 children with paravertebral malignant tumors. In our study, approximately 80% of patients had complaints of pain, motor deficits (paralysis or plegia), and deep tendon reflex changes at diagnosis. The high rate of neurological deficits was presumably due to delays in referral to pediatric oncology centers. Pediatric and/or non-pediatric physicians (orthopedics/neurosurgery/pediatric surgery) should be aware that all children experiencing back and/or extremity pain should have a thorough neurological and systemic assessment. Neurological findings of tilt symptoms, which were also present in two of our patients, in cervical spinal masses should be recognized by physicians. It is not easy for the family to notice the swelling in the sacrococcygeal region for germ cell tumors. We would also like to emphasize that it is important to remove the diapers of infants to perform a detailed examination. Since cord compression may be a finding in acute leukemia/lymphomas, the presence of hepatosplenomegaly, all regional lymph node examinations, and laboratory tests are important.[19,20] It must be known that a detailed evaluation is the cornerstone of the diagnosis.

Magnetic resonance imaging (MRI) is known as the most effective imaging method for the spinal cord and canal and also provides information about the origin of the tumor.[21,22] MRI was performed on almost all of our patients; however, computerized tomography was used when emergency MRI with anesthesia was not possible and /or before the 2000s in our center. We found the most common spinal cord compression in the thoracic region. It is important to note that an MRI should be done within 24-48 hours as irreversible permanent neurological sequelae may develop in children.

Treatment options for a patient presenting with spinal cord compression include anti-edema (steroid) therapy and tumor specific therapy like surgery, chemotherapy, and radiation therapy.[1,5,11] Although there is no clear information about the superiority of these treatment methods over each other, a multidisciplinary approach may be required depending on the type of tumor.[9,22,23] The histopathological diagnosis of the tumor is the determinant in the selection and success of the treatment.[14,24] High-dose dexamethasone reduces vasogenic cord edema and provides neurological improvement. In our series, approximately 90% of the patients were treated with steroids as anti-edema therapy. Since the patients had chemosensitive and high-grade tumors in this study, approximately 70% of the patients received chemotherapy according to the histopathological diagnosis and stage. Surgery may be required according to the histopathological diagnosis and/or progression of neurological findings despite chemotherapy and dexamethasone treatment for cord compression.[10,22,25] Surgery was performed in 39 patients in our study, and decompressive surgery and laminectomy (35%) were most commonly performed due to poor neurological clinical course. If the tumor is radioresponsive, radiation therapy is often the choice of treatment.[16,23] In the literature, 180-400cGy radiotherapy is recommended in radiosensitive tumors to provide spinal decompression.[9,16]

But we could not evaluate the dose or late sequels of radiotherapy given for compression due to the non-specificity of the study group. Because spinal radiotherapy was given to 35 (48%) patients according to whether the patients had previously received spinal radiotherapy, histopathology of the tumor, and progression of neurological findings in our series. Even though 22 patients with CNS tumors with spinal metastases received radiotherapy, 18 of them died due to the rapid progression of the disease. Spinal cord surgery and radiotherapy could cause serious growth problems, late side effects, and orthopedic spine defects in children, and 6 patients in our study had to use orthotic devices owing to spinal deformities. As our patients had wide heterogeneity in diagnosis, histologic classification, stage, treatment methods, and prognoses, we could not determine the best treatment. Moreover, spinal cord compression treatment requires a multidisciplinary approach in childhood cancers.

We found that the mean time to diagnosis was 27 days, but the duration of symptoms before diagnosis prolonged to 150 days in this study. Complete neurological recovery was achieved in 33 (45%) patients in the present series of patients. Tantawy et al.[25] found that neuroblastoma (29.2%) was the most common cause of malignant cord compression and reported that the time from symptom to diagnosis was 42 days and 75% of the patients had complete neurological improvements. They observed a high neurological recovery rate despite the delayed diagnosis due to their patients having chemosensitive tumors such as neuroblastoma and lymphoma. Furthermore, Kurucu et al.[12] reported that complete and partial recovery of neurologic deficits was achieved in 56% of patients with lymphomas in the literature. Unfortunately, we found that clinical neurologic sequelae were permanent in 55% of our patients. The high rate of permanent sequelae can be explained by the delay in diagnosis as well as the heterogeneity of histologic classification. One-third of the patients with high-grade CNS tumors were resistant to combined treatment, and also these patients had spinal metastases.

In our series, the mean follow-up period of the patients was 3.26±4.90 years (0.1-22 years). The 5-year overall survival rates for high-grade CNS tumors with intradural compression, and solid tumors with extradural compression were 22%, and 62%, respectively. Survival rates were similar to the literature in spinal cord compression due to extradural tumors.[18,25] But, the low survival rate of tumors with intradural compression might be explained by the high rate of metastatic CNS tumors in this series.

The spinal cord compression is an oncological emergency as irreversible permanent sequelae may develop. Physicians need to be made aware of symptoms owing to the important of early diagnosis and the effectiveness of urgent anti-edema treatment in cord compression.

The most important factors affecting the success of treatment for cord compression are early diagnosis and urgent treatment. It must be emphasized that back pain and extremity pain should be considered symptoms of cord compression. For this reason, every physician should perform a detailed systemic and neurological examination. In this study, we aimed to emphasize that delay in diagnosis or failure to manage or recognize symptoms may be important risk factors for permanent neurological sequelae. However, studies which are prospective, multicenter, and include patients with the same histological diagnosis are necessary to determine the most important prognostic factor and treatment.

Ethical approval

Gazi University Ethics Committee approved the study (report number: 2017120103-2).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: AO, FGP; data collection: AO, ÖV; analysis and interpretation of results: AO, ÖV, FGP; draft manuscript preparation: ÖV. All authors reviewed the results and approved the final version of the manuscript.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Freedman JL, Rheingold SR. Fisher MJ. Oncologic emergencies. In: Pizzo PA, Poplack DG, editors. Principles and Practice of Pediatric Oncology (7th ed). Philadelphia: Wolters Kluwer; 2016: 980-982.
2. De Martino L, Spennato P, Vetrella S, et al. Symptomatic malignant spinal cord compression in children: a single-center experience. Ital J Pediatr 2019; 45: 80. https://doi.org/10.1186/s13052-019-0671-5
3. Aydin GB, Kutluk MT, Buyukpamukcu M, Akyuz C, Yalcin B, Varan A. Neurological complications of neuroblastic tumors: experience of a single center. Childs Nerv Syst 2010; 26: 359-365. https://doi.org/10.1007/s00381-009-0979-3
4. Chintagumpala MM, Paulino A, Panigrahy A, Hawkins C, Jae A, Parsons W. Embryonel and pineal region tumors. In: Pizzo PA, Poplack DG, editors. Principles and Practice of Pediatric Oncology (7th ed). Philadelphia: Wolters Kluwer; 2016: 671-680.
5. Katzenstein HM, Kent PM, London WB, Cohn SL. Treatment and outcome of 83 children with intraspinal neuroblastoma: the Pediatric Oncology Group experience. J Clin Oncol 2001; 19: 1047-1055. https://doi.org/10.1200/JCO.2001.19.4.1047
6. Demir HA, Yalçin B, Büyükpamukçu N, et al. Thoracic neuroblastic tumors in childhood. Pediatr Blood Cancer 2010; 54: 885-889. https://doi.org/10.1002/pbc.22405
7. Mullen E, Whangbo J, Vrooman LM. Oncologic emergencies. In: Orkin S, Fisher D, Look TA, et al., editors. Oncology of Infancy and Childhood. Philadelphia: Saunders Elsevier; 2009: 1122-1128. https://doi.org/10.1016/B978-1-4160-3431-5.00028-5
8. De Bernardi B, Pianca C, Pistamiglio P, et al. Neuroblastoma with symptomatic spinal cord compression at diagnosis: treatment and results with 76 cases. J Clin Oncol 2001; 19: 183-190. https://doi.org/10.1200/JCO.2001.19.1.183
9. Robinson CG, Prayson RA, Hahn JF, et al. Long-term survival and functional status of patients with low-grade astrocytoma of spinal cord. Int J Radiat Oncol Biol Phys 2005; 63: 91-100. https://doi.org/10.1016/j.ijrobp.2005.01.009
10. Mohme M, Mende KC, Krätzig T, et al. Impact of spinal cord compression from intradural and epidural spinal tumors on perioperative symptoms-implications for surgical decision making. Neurosurg Rev 2017; 40: 377-387. https://doi.org/10.1007/s10143-016-0790-z
11. Gunes D, Uysal KM, Cetinkaya H, et al. Paravertebral malignant tumors of childhood: analysis of 28 pediatric patients. Childs Nerv Syst 2009; 25: 63-69. https://doi.org/10.1007/s00381-008-0717-2
12. Kurucu N, Akyüz C, Varan A, et al. Primary paraspinal and spinal epidural non-hodgkin lymphoma in childhood. J Pediatr Hematol Oncol 2021; 43: e395-e400. https://doi.org/10.1097/MPH.0000000000001858
13. Yon DK, Ahn TK, Shin DE, Kim GI, Kim MK. Extragonadal germ cell tumor of the posterior mediastinum in a child complicated with spinal cord compression: a case report. BMC Pediatr 2018; 18: 97. https://doi.org/10.1186/s12887-018-1070-6
14. Li Z, Lv Z, Yang Q, Li J. Successful treatment of a primary thoracic dumb-bell yolk sac tumor presenting with severe spinal cord compression: case report. Medicine (Baltimore) 2019; 98: e17610. https://doi.org/10.1097/MD.0000000000017610
15. Kutluk T, Varan A, Kafalı C, et al. Pediatric intramedullary spinal cord tumors: a single center experience. Eur J Paediatr Neurol 2015; 19: 41-47. https://doi.org/10.1016/j.ejpn.2014.09.007
16. Houten JK, Weiner HL. Pediatric intramedullary spinal cord tumors: special considerations. J Neurooncol 2000; 47: 225-230. https://doi.org/10.1023/a:1006418506213
17. Cambruzzi E, Medeiros MS, Cardoso CE, Silva GAG, Schlotte K, Kus WP. Diffuse leptomeningeal glioneuronal tumor in an 8-year-old girl: case report and review of the literature. Childs Nerv Syst 2023; 39: 301-305. https://doi.org/10.1007/s00381-022-05625-1

18. Tang J, Zhang D, Xu YY, et al. Clinical characteristics and therapeutic outcomes of mediastinal neuroblastoma with intraspinal extension: a retrospective study. Transl Pediatr 2021; 10: 715-722. https://doi.org/10.21037/tp-20-268

19. Chapman S, Li J, Almiski M, Moffat H, Israels SJ. Epidural spinal mass as the presenting feature of b-acute lymphoblastic leukemia in a young child. J Pediatr Hematol Oncol 2020; 42: e845-e847. https://doi.org/10.1097/MPH.0000000000001609

20. Boushra M. A case report of b-cell lymphoblastic leukemia/lymphoma presenting as isolated torticollis in a 2-year-old female. Clin Pract Cases Emerg Med 2020; 4: 603-606. https://doi.org/10.5811/cpcem.2020.8.48524

21. Gao H, Wan Y, Ma H, Huang T, Song W. Neuroendocrine tumor of thoracic spine: case report and literature review. Transl Cancer Res 2021; 10: 1177-1182. https://doi.org/10.21037/tcr-20-2279

22. Kpelao E, Doleagbenou AK, El Kader Moumouni A, et al. Spinal cord compression in Togo: etiologies and management. World Neurosurg 2022; 162: e542-e545. https://doi.org/10.1016/j.wneu.2022.03.063

23. McGirt MJ, Chaichana KL, Atiba A, et al. Incidence of spinal deformity after resection of intramedullary spinal cord tumors in children who underwent laminectomy compared with laminoplasty. J Neurosurg Pediatr 2008; 1: 57-62. https://doi.org/10.3171/PED-08/01/057

24. Pollono D, Tomarchia S, Drut R, Ibañez O, Ferreyra M, Cédola J. Spinal cord compression: a review of 70 pediatric patients. Pediatr Hematol Oncol 2003; 20: 457-466.

25. Tantawy AA, Ebeid FS, Mahmoud MA, Shepl OE. Spinal cord compression in childhood pediatric malignancies: multicenter egyptian study. J Pediatr Hematol Oncol 2013; 35: 232-236. https://doi.org/10.1097/MPH.0b013e318270b210